UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/786,720	02/26/2004	Margot Mary O'Toole	AM101329	2740

25291 7590 12/05/2008

WYETH
PATENT LAW GROUP
5 GIRALDA FARMS
MADISON, NJ 07940

EXAMINER	
MYERS, CARLA J	

ART UNIT	PAPER NUMBER
1634	

MAIL DATE	DELIVERY MODE
12/05/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/786,720	O'TOOLE ET AL.	
	Examiner	Art Unit	
	Carla Myers	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 September 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *20-29* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *20-29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on September 26, 2008 has been entered.

2. Claims 20-29 are pending and have been examined herein. The following includes new grounds of rejection necessitated by Applicant's amendments to the claims. This action is made non-final.

Claim Rejections - 35 USC § 112, first paragraph – New Matter

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 21 and 23-29 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

The specification as originally filed does not appear to provide support for the subject matter of newly added claims 21 and 23-29.

Regarding claim 21, the specification as originally filed does not provide support for the recitation in newly added claim 21 of a method comprising determining and comparing the expression of mouse SFRP1 mRNA by direct sequencing or column chromatography. In the reply of July 3, 2008, Applicants point to paragraph [0175] as providing support for this amendment. However, paragraph [0175] is directed to methods for the detection of specific polynucleotide molecules. This paragraph does not particularly address methods for detecting the expression level of SFRP1 mRNA. While the specification indicates that methods such as column chromatography and direct sequencing can be used to detect a specific polynucleotide sequence, these teachings do not provide support for the distinct concept of determining and comparing the expression of mouse SFRP1 mRNA (i.e., determining the quantity or level of mouse SFRP1 mRNA) by direct sequencing or column chromatography, as is encompassed by newly added claim 21.

Regarding claims 23 and 24, the specification as originally filed does not appear to provide support for the recitation that the agent is a ribozyme and that the ribozyme is an interfering RNA (claim 23) or an siRNA (claim 24). In the response of July 3, 2008, Applicants point to paras [0096-0099] as providing support for these claims. The cited passages provide support only for the concept of an interfering RNA or a siRNA. The cited passages do not, however, provide support for distinct concept that the agent is a ribozyme and that the ribozyme is an interfering RNA or an siRNA.

Regarding claims 25-28, the specification as originally filed does not appear to provide support for the subject matter of these claims. In the reply of July 3, 2008,

Applicants point to paras [0181-0183] as providing support for claims 25-28. However, while the specification provides support for the concept that an agent may be a small molecule or bioactive agent and for the concept of an agent that modulates the binding of SFRP to a binding partner, the specification does not appear to provide support for the concept that the agent is specifically an agent that modulates binding of SFRP1 mRNA to a binding partner. That is, the teachings in the specification cited by Applicants are directed to agents that are inhibitors of LRPs proteins. These passages do not appear to be directed to agents that modulate SFRP1 mRNA. Accordingly, the specification also does not appear to provide support for newly added claims 25-28.

Regarding claim 29, the specification as originally filed does not appear to provide support for the concept of a method comprising administering an agent to a mouse with lupus and determining if the agent modulates expression of the mouse SFRP1 mRNA, wherein the agent "modifies the mouse SFRP1 mRNA to improve its stability or solubility." The response of July 3, 2008 points to paragraph [0113] as providing support for this amendment. However, paragraph [0113] is not directed to agents to be used in screening assays. Rather, paragraph [0113] is directed to polynucleotides that have themselves been modified at the base moiety, sugar moiety or phosphate backbone to improve the stability, hybridization or solubility of the polynucleotide. Accordingly, the specification as originally filed does not appear to provide basis for the concept set forth in newly added claim 29 of a method of administering to a mouse an agent that "modifies the mouse SFRP1 mRNA to improve its stability or solubility."

Claim Rejections - 35 USC § 112, first paragraph – Written Description

4. Claims 25-29 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a Written Description rejection.

In analyzing the claims for compliance with the written description requirement of 35 U.S.C. 112, first paragraph, the written description guidelines note that with regard to genus/species situations, a "Satisfactory disclosure of a "representative number" depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed." To ascertain whether the written description requirement is met for a genus claim, it is first determined whether a representative number of species have been described by their complete structure. It is then determined whether a representative number of species have been defined by other identifying characteristics.

In the present situation, the claims are drawn to methods comprising administering an agent to a mouse with lupus and comparing expression of mouse SFRP1 mRNA in kidney samples of the mouse before and after said administering to determine if said agent modulates expression of mouse SFRP1, wherein said agent modulates binding of SFRP1 mRNA to a binding partner (claim 25) AND is a small molecule (claim 26), a bioactive agent (claim 27), or a bioactive agent present in a

pharmaceutical composition (claim 28), or wherein said agent modifies SFRP1 mRNA to improve its stability or solubility.

The claimed genus of agents is considered to be significantly large since the claims encompass agents that may be naturally occurring or synthesized, agents that are inorganic, protein, nucleic acid or carbohydrate molecules, agents of any size or mass, etc.

The specification does not describe agents that modulate binding of SFRP1 mRNA to a binding partner or which improve the stability or solubility of SRFP1 mRNA in terms of their complete structure.

Further, no agents which modulate binding of SFRP1 mRNA to a binding partner or which improve the stability or solubility of SRFP1 mRNA have been sufficiently described in terms of any other relevant identifying characteristics.

Thus, Applicant has not established that they were in possession of a representative number of agents that modulate binding of SFRP1 mRNA to a binding partner or agents which improve the stability or solubility of SRFP1 mRNA.

As set forth in *Rochester,* 358 F.3d at 923; *Eli Lilly*, 119 at 1568, the "disclosure must allow one skilled in the art to visualize or recognize the identity of the subject matter purportedly described." *Id.* Not all functional descriptions "necessarily fail as a matter of law to meet the written description requirement; rather, the requirement may be satisfied if in the knowledge of the art the disclosed function is sufficiently correlated to a particular, known structure." *Amgen Inc. v. Hoechst Marion Roussel, Inc.*, 314 F.3d 1313, 1332 (Fed. Cir. 2003).,

However, in the present situation, the specification does not disclose a clear structure-function relationship between the agents and the functional activities of modulating binding of SFRP1 mRNA to a binding partner or improving the stability or solubility of SRFP1 mRNA. In the absence of any real structure-function relationship and in the absence of a representative number of species of the claimed genus, there is insufficient descriptive support for the currently claimed genus of agents.

Further, "Possession may not be shown by merely describing how to obtain possession of members of the claimed genus or how to identify their common structural features. *See University of Rochester*, 358 F.3d at 927, 69 USPQ2d at 1895." Thereby, a showing of how to potentially identify and make agents that modulate binding of SFRP1 mRNA to a binding partner or which improve the stability or solubility of SRFP1 mRNA is not sufficient to establish that Applicant's were in possession of the invention as broadly claimed.

The decisional law in this area has been very consistent. The Federal Circuit in Lilly, Fiers, Rochester and many other cases has determined that the written description issue applies to situations where the definition of the subject matter of the claims fails to provide description commensurate with the genus. The most recent case law directly supports this rejection. As the District Court in University of Rochester v. G.D. Searle & Co., Inc. (2003 WL 759719 W.D.N.Y.,2003. March 5, 2003.) noted "In effect, then, the '850 patent claims a method that cannot be practiced until one discovers a compound that was not in the possession of, or known to, the inventors themselves. Putting the claimed method into practice awaited someone actually discovering a necessary

component of the invention." This is similar to the current situation since the breadth of the current claims comprises the use of agents which the present inventors were not in the possession of, or which were not known to the inventors. In a genus that is possibly quite immense, the specification does not disclose a single example of an agent that modulates binding of SFRP1 mRNA to a binding partner or an agent which improves the stability or solubility of SRFP1 mRNA.

As noted in Vas-Cath Inc. v. Mahurkar (19 USPQ2d 1111, CAFC 1991), the Federal Circuit concluded that:

"...applicant must also convey, with reasonable clarity to those skilled in art, that applicant, as of filing date sought, was in possession of invention, with invention being, for purposes of "written description" inquiry, whatever is presently claimed."

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. 112 is severable from its enablement provision.

With respect to the present invention, there is no record or description which would demonstrate conception of a representative number of agents that modulate binding of SFRP1 mRNA to a binding partner or which improve the stability or solubility of SRFP1 mRNA. Therefore, the claims fail to meet the written description requirement because the claims encompass a significantly large genus of polynucleotide sequences which are not described in the specification.

Claim Rejections - 35 USC § 112 - Enablement

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 25-29 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The following factors have been considered in formulating this rejection (*In re Wands*, 858F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988): the breadth of the claims, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art, the amount of direction or guidance presented, the presence or absence of working examples of the invention and the quantity of experimentation necessary.

Breadth of the Claims:

The claims are drawn to methods comprising administering an agent to a mouse with lupus and comparing expression of mouse SFRP1 mRNA in kidney samples of the mouse before and after said administering to determine if said agent modulates expression of mouse SFRP1, wherein said agent modulates binding of SFRP1 mRNA to a binding partner (claim 25) AND is a small molecule (claim 26), a bioactive agent (claim 27), or a bioactive agent present in a pharmaceutical composition (claim 28), or wherein said agent modifies SFRP1 mRNA to improve its stability or solubility.

The claimed genus of agents is considered to be significantly large since the claims encompass agents that may be naturally or non-naturally occurring, agents that

are inorganic, protein, nucleic acid or carbohydrate molecules, agents of any size or mass, etc.

Nature of the Invention

The claims encompass methods for determining if an agent modulates expression of SRFP1 by comparing mRNA expression levels in kidney tissues from mice before and after treatment with an agent. The invention is in a class of inventions which the CAFC has characterized as 'the unpredictable arts such as chemistry and biology" (Mycolgen Plant Sci., Inc. v. Monsanto Co., 243 F.3d 1316, 1330 (Federal Circuit 2001)).

Teachings in the Specification and State of the Art:

The specification does not describe agents that modulate binding of SFRP1 mRNA to a binding partner or which improve the stability or solubility of SRFP1 mRNA in terms of their complete structure.

Regarding agents that effect protein activity, the specification (paras [0181-0183]) teaches the general concept that an agent may be a small molecule or bioactive agent and that an agent may modulate the binding of SFRP protein to a binding partner. However, the specification does not disclose the specific structure of any such agents. Also, these teachings are limited to the SFRP1 protein and not the SRFP1 mRNA.

Further, regarding claim 29, the specification (para [0113]) teaches the concept that a polynucleotide may be modified at the base moiety, sugar moiety or phosphate backbone to improve the stability, hybridization or solubility of the polynucleotide. However, the specification does not disclose any particular agents that may be

administered to a mouse and which modify SFRP1 mRNA to thereby improve its stability or solubility.

The Predictability or Unpredictability of the Art and Amount of Direction or Guidance Provided by the Specification:

The claims require the use of particular agents which have the properties of modulating the binding of SFRP1 mRNA to a binding partner or improving the stability or solubility of SFRP1 mRNA. However, the art of identifying novel agents that modulate binding of SFRP1 mRNA to a binding partner or which improve the stability or solubility of SRFP1 mRNA is highly unpredictable.

The specification does not provide any information regarding a structure-function relationship between the agents and their activity of modulating binding of SFRP1 mRNA to a binding partner or improving the stability or solubility of SRFP1 mRNA. There is also no information in the specification as to the identity of molecules that bind to SFRP1, and thereby whose binding can be increased or decreased by administering an agent to a mouse. There is also no information provided in the specification regarding the stability or solubility of SFRP1 mRNA in kidney cells or tissues, and/or as to the type of agent that might increase or decrease (and thereby "improve") the stability or solubility of SFRP1 mRNA. Thereby, it is highly unpredictable as to what would be the structure of such agents.

The specification does not provide any specific guidance as to how to predictably identify agents that modulate binding of SFRP1 mRNA to a binding partner or which improve the stability or solubility of SRFP1 mRNA. There is no guidance provided in the

specification as to the types of molecules that might have this particular activity. For example, there is no information provided in the specification as to whether the agents would be proteins or nucleic acids or carbohydrates or inorganic compounds, or whether the agents bind to SFRP1 mRNA or chemically modify SFRP1 mRNA, etc. There is also no guidance provided in the specification as to how to administer any type of agent of any chemical composition to a mouse so that the agent effectively reaches the kidneys of mice, so as to permit the agent to modulate or not modulate the expression of mouse SFRP1 mRNA. No information is provided in the specification regarding the route of administration, the quantity of agent, etc. for the widely diverse types of agents encompassed by the claims.

Quantity of Experimentation:

In the absence of any specific guidance provided in the specification as to the structural features of the agents encompassed by the claims and in the absence of a relationship between the structure of agents and their activity of modulating binding of SFRP1 mRNA to a binding partner or improving the stability or solubility of SRFP1 mRNA, undue experimentation would be required to practice the claimed invention. While methods are known in the art for determining if an agent modulates binding of SFRP1 mRNA to a binding partner or modulates mRNA solubility or stability, such methods provide only the general guidelines that allow researchers to randomly search for agents having the properties of modulating binding of SFRP1 mRNA to a binding partner or improving the stability or solubility of SRFP1 mRNA. The results of performing such methodology are highly unpredictable. The specification has provided

only an invitation to experiment. The specification does not provide a predictable means for identifying and using a representative number of the diverse agents encompassed by the claims.

Working Examples:

The specification does not provide any working examples of a method in which an agent is administered to a mouse with lupus and the expression of mouse SFRP1 mRNA in kidney samples of the mouse is determined, wherein the agent is one which modulates binding of SFRP1 mRNA to a binding partner or improves the stability or solubility of SRFP1 mRNA.

Conclusions:

Case law has established that '(t)o be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without 'undue experimentation.'" *In re Wright* 990 F.2d 1557, 1561. *In re Fisher,* 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) it was determined that '(t)he scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification to persons of ordinary skill in the art". The amount of guidance needed to enable the invention is related to the amount of knowledge in the art as well as the predictability in the art. Furthermore, the Court in *Genetech Inc. v Novo Nordisk* 42 USPQ2d 1001 held that '(I)t is the specification, not the knowledge of one skilled in the art that must supply the novel aspects of the invention in order to constitute adequate enablement".

In the present application, the specification does not provide sufficient information regarding the structure of agents that modulate binding of SFRP1 mRNA to a binding partner or which improve the stability or solubility of SRFP1 mRNA. No examples of provided for such agents and no guidance is provided in the specification as to how to obtain such agents. In view of the unpredictability in the art, and the lack of disclosure in the specification and in the prior art and the unpredictability of the art, it would require undue experimentation for one of skill in the art to make and use the invention as broadly claimed.

Claim Rejections - 35 USC § 112 second paragraph

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 20-29 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 20-29 are indefinite over the recitation of "the mouse SFRP1" because this phrase lacks proper antecedent basis. While the claims previously refer to mouse SFRP1 mRNA, the claims do not previously refer to "the mouse SFRP1." Also, the claims are indefinite because the claims omit the essential steps required to accomplish the step of determining if the agent modulates expression of mouse SFRP1 (i.e., mouse SFRP1 protein). While the claims recite a step of comparing expression of mouse SFRP1 mRNA levels in kidney samples, the claims do not recite any particular steps of

determining mouse SFRP1 protein levels. This rejection may be overcome by amendment of the claims to recite in claim 20, line 4 "the mouse SFRP1 mRNA."

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Carla Myers whose telephone number is 571-272-0747. The examiner can normally be reached on Monday-Thursday (6:30-5:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on 571-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Carla Myers/
Primary Examiner, Art Unit 1634